INTEGRATED BIO-REACTOR MONITOR AND CONTROL SYSTEM

Background of the Invention

Field of the Invention

[0001] This invention relates to systems and methods for managing process conditions in a container or chamber, including controlling bioreactors for cell cultures and microbial fermentation, semiconductor fabrication and liquid chromatography.

Description of the Related Art

[0002] Many manufacturing and biological generation processes consist of a complex sequence of steps and require positive control over environmental conditions to consistently reproduce a desired result. In cell culture growth, for example, geneticists manipulate DNA by identifying, excise, move and place genes into a variety of cells that are genetically quite different from the source cell, and these recombinant cells can produce proteins that may be of immense commercial value. Once the gene is successfully transferred to another cell, the growth process for the cell must be closely monitored and controlled to provide an effective environment that promotes cell viability. Understanding and documenting environmental conditions affecting the viability of cells, and accurately controlling such conditions allows consistent reproduction of the cell culture process.

[0003] Cell culture processes are commonly developed and optimized in a benchtop scaled bioreactor, and then be scaled-up to a large production process according to commercial demands. The process may take weeks or even months, and include numerous changes to the conditions of the media, or solution, contained in the bioreactor during this period. For example, desired conditional changes to the solution can include adjustments to pH, temperature, and dissolved oxygen. Providing precise amounts of certain fluids or gasses to the bioreactor, either directly or indirectly (e.g., using fluids to heat or cool a solution) changes these and other conditions of the solution. Typically, monitoring a process is accomplished by entering data from a bioreactor sensor into a logbook, from time-to-time. Agitating the solution, or adding fluids or gasses to the solution, is also generally done

manually in an amount estimated by the attending operator, and recorded in a paper logbook. Poor documentation and/or imprecisely adding fluid or gas to the process can result in an unacceptably high level of uncertainty as to the steps required for the process, thereby making a faithful reproduction of the process nearly impossible.

[0004] Additionally, government regulation of certain manufacturing processes may require implementation of strict documentation and control procedures. For example, the Food and Drug Administration's (FDA's) 21 Code of Federal Regulations Part 11 applies to records in electronic form that are created, modified, maintained, archived, retrieved, or transmitted under any records requirement set forth in Agency regulations, and to electronic records submitted to the Agency under the Federal Food, Drug, and Cosmetic Act an the Public Health Service Act. Part 11 includes provisions related to limiting system access to authorized individuals, use of operational checks, use of authority checks, and use of electronic signatures. As biological control systems move towards electronic implementations, it is advantageous to design systems to easily incorporate regulations governing electronic records and control procedures.

Summary of the Invention

[0005] This invention relates to systems and methods for managing process conditions in a container or chamber, including controlling bioreactors for cell cultures and microbial fermentation, controlling semiconductor fabrication and controlling liquid chromatography. According to one embodiment, the invention comprises a system for controlling a plurality of different bioreactor processes in a plurality of bioreactors, comprising a first communication network, a second communication network, a first bioreactor configured to send a first data signal related to a condition in said first bioreactor, a second bioreactor configured to send a second data signal related to a condition in said second bioreactor, a utility tower, coupled to said first and second bioreactors, configured to receive the first and second data signals and send first information based on the first data signal and second information based on the second data signal over said first network, and configured to receive a first control signal for said first bioreactor and a second control signal for said second bioreactor over said second network and change a condition in said first

bioreactor based on the first control signal and change a condition in said second bioreactor based on the second control signal, and a controller, connected to said utility tower by said first and second network, configured to receive the information from said utility tower over said first network, determine the first control signal based on a first bioreactor process and/or the first information, and determine the second control signal based on the second bioreactor process and/or the second information, and send the first and second control signals to said utility tower over said second network.

[0006] According to another embodiment, the invention comprises a system for controlling a bioreactor process, comprising a communication system, a controller configured to receive information related to a condition in a bioreactor, to control the bioreactor process by determining control signals based on the bioreactor process, and to send the control signals over said communication system, and a utility tower, coupled to said controller via said communication system, configured to receive the control signals and to change a condition in the bioreactor based on the control signals, said utility tower comprising a monitoring system that transmits information related to a condition of the bioreactor to said controller via said communication system, a bioreactor supply system which supplies a substance to the bioreactor in response to a control signal, and an agitation system which agitates the solution in the bioreactor in response to a control signal.

[0007] According to yet another embodiment, the invention comprises a method of controlling a benchtop bioreactor with a controller configured with a sequence of steps and parameters of a bioreactor process and coupled to a bioreactor utility tower via a communication system, comprising determining a control action to change a condition in the bioreactor based on the sequence of steps of the bioreactor process, sending a first signal from the controller to the bioreactor utility tower over the communication system to direct the bioreactor utility tower to perform a first control action, and performing the first control action to change the condition in the bioreactor.

[0008] According to yet another embodiment, the invention comprises a system for controlling a bioreactor process, comprising means for determining a control action to change a condition in the bioreactor based on the sequence of steps of the bioreactor process, means for sending a first signal from the controller to the bioreactor utility tower over the

communication system to direct the bioreactor utility tower to perform a first control action, and means for performing the first control action to change the condition in the bioreactor.

[0009] In another embodiment, the invention comprises a system for monitoring and controlling a process in a controlled chamber, the process comprising a sequence of steps and at least one parameter relating to a condition of the process, comprising a communication system, a controller configured to receive information related to a condition in the chamber, to control the chamber process by determining a control action required to carry out the process based on the chamber process steps and the received information, to generate a control signal corresponding to the control action, and to send the control signal over said communication system, and a utility tower, coupled to said controller via said communication system, configured to provide information related to a condition in the chamber to said controller via said communication system, to receive the control signal from said controller and to change a condition of the chamber based on the control signal, said utility tower comprising a monitoring system that transmits information related to a condition of the chamber to said controller via said communication system, and a chamber supply system which supplies a substance to the bioreactor in response to the control signal.

[0010] In yet another embodiment, the invention comprises a program storage device readable by a machine, tangibly embodying a program of instructions executable by the machine to perform a method of controlling a benchtop bioreactor with a controller configured with a sequence of steps and parameters of a bioreactor process and coupled to a bioreactor utility tower via a communication system, the method comprising receiving a measurement signal indicating a condition in the benchtop bioreactor at the bioreactor utility tower, transmitting information related to the condition from the utility tower to the controller over the communication system, comparing the information to a parameter of the bioreactor process to determine a control action, sending a signal from the controller to the bioreactor utility tower via the communication system to control the bioreactor utility tower to perform the control action, and performing the control action to change the condition in the bioreactor.

Brief Description of the Drawings

[0010] The above-mentioned and other features and advantages of the invention will become more fully apparent from the following detailed description, the appended claims, and in connection with the accompanying drawings in which:

[0011] Figure 1 is a block diagram of a control system.

[0012] Figure 2 is a more detailed block diagram of the utility tower part in the control system.

[0013] Figure 3 is a block diagram of a gas control system.

[0014] Figure 4 is a block diagram of a pump control system.

[0015] Figure 5 is a functional block diagram of the controller.

[0016] Figure 6 is a functional block diagram of the computer contained in the utility tower.

[0017] Figure 7 is a block diagram showing control systems networked together.

Detailed Description

[0018] Embodiments of the invention will now be described with reference to the accompanying Figures, wherein like numerals refer to like elements throughout. The terminology used in the description presented herein is not intended to be interpreted in any limited or restrictive manner, simply because it is being utilized in conjunction with a detailed description of certain specific embodiments of the invention. Furthermore, embodiments of the invention may include several novel features, no single one of which is solely responsible for its desirable attributes or which is essential to practicing the inventions herein described. The scope of the invention should therefore be construed in accordance with the appended claims and any equivalents thereof.

[0019] Figure 1 is a high-level block diagram of a control system 100. The control system described herein has numerous control applications, including controlling chambers, or processing areas where it is useful to have precise monitoring and application of gasses, fluids and solids. Examples of these application areas include, for example, high performance liquid chromatography, semiconductor fabrication, foods, beverages, petroleum, chemicals, cell cultures and microbial fermentation.

[0020] In this embodiment, the control system 100 is shown to inter-operate with two bioreactors 105, 110 which are controlled by a utility tower 115 and a controller 120. Although shown as separate units in this example, the controller 120 and the utility tower 115 can also be contained in the same unit. The bioreactors 105, 110 can be any of a number of types of bioreactors implementing a controlled process that benefits from monitoring conditions of the process and controlling factors affecting the process, for example, microbial fermentation and cell cultures.

[0021] The bioreactors 105, 110 typically include a suitable container or vessel, and a headplate, which has connections 170, 175 to the utility tower 115. Although the connections 170, 175 are depicted only by a single line, the connections 170, 175 may include numerous wires, tubes or other means for communicating information or for transferring material, for example, fluids, solids, or gases, between the utility tower 115 and the bioreactors 105, 110. The bioreactors 105, 110 can be monitored by sensors that measure the conditions (e.g., temperature, pH, dissolved oxygen, and level/foam) in the bioreactor at specified times or continuously, and use the connections 170, 175 to the utility tower for communicating sensor information. The connections 170, 175 can include gas lines that provide gas from the utility tower 115 to the head space of the vessel and/or to sparge, i.e., near the bottom of the vessel so that the gas is emitted into a solution contained in the vessel. Such gasses can include, for example, nitrogen, oxygen, air, and carbon dioxide, or another gas as required for a particular application.

[0022] The connections 170, 175 can also include tubes that carry fluids from the utility tower 115 to the bioreactors 105, 110. Fluids, for example, reagents, can be provided directly into the vessel to chemically change the solution, or, fluids can be used to indirectly affect the process, for example the fluids can be used with a heating/cooling jacket. The utility tower 115 can also use the connections 170, 175 to communicate control signals to other devices that may be used to affect the bioreactors 105, 110, for example, an agitation motor, and optical density, carbon dioxide, and glucose measurement devices.

[0023] The utility tower 115 includes devices, e.g., transmitters, that receive sensor data from sensors within the bioreactors 105, 110 and transmit information relating to the sensor data to a controller 120. The utility tower 115 is also configured with devices to

receive information from controllable devices or equipment in, or attached to, the utility tower 115 and transmit the information to a controller 120. The utility tower 115 can include a human-machine interface ("HMI") 125 that provides information to an operator of the control system. The HMI 125 can be configured to display information related to particular part of the control system 100, or information related to several areas of the control system or information relating to the entire control system. The HMI 125 can be a display screen or a touch-screen display that can be used to interactively enter commands for the control system. In another embodiment, the utility tower 115 does not include a HMI 125. Instead, visual information is provided to the operator on a display screen at the controller 120, or at a remote device, e.g., wireless device 155 or another computer (not shown) in communication with the utility tower 115.

[0024] The utility tower 115 can include an interface 150 that provides a suitable connection for various devices, e.g., a keyboard 130, and other peripheral devices (not shown), e.g., a mouse, a printer, a local area network ("LAN"), and/or a modem. In one example, the interface 150 includes a USB port. In one embodiment, the utility tower 115 includes an interface (not shown) that allows communication with a wireless computing device 155, e.g., a wireless tablet PC. Using the wireless computing device 155, a user can remotely monitor the control system by receiving information via a wireless connection 160 from the utility tower 115 and/or change the control functionality by sending commands via the wireless link 160 to the utility tower 115.

[0025] A user can input information into the process control system 100 using a device such as a mouse and/or a keyboard, or by using the touch-screen HMI 125, if the utility tower 115 is so configured. The utility tower 115 can be configured without a display screen, for example, when a plurality of utility towers are connected on a network, discussed further below. In a network configuration, at least one of the utility towers will typically have a display screen to allow the user to receive the system information, or there will be another display device in the control system that conveys information relating to the control system 100 to a user.

[0026] The network connections 135, 140, 145, which may also be referred to herein as busses or networks, provide three communication channels, in this example, between

the utility tower 115 and the controller 120. In other example configurations, there can be more or fewer network connections between the utility tower and the controller 120. In one example configuration, communications described herein as using network connection 135 and the network connection 140 can use the same network connection between the utility tower 115 and the controller 120, assuming, of course, the utility tower 115 is configured with suitable devices that can communicate via the same network bus. In another example configuration, the utility tower 115 can use one bidirectional bus to communicate with the controller 120. Network connections between the utility tower 115 and the controller 120 may also be referred to individually herein as a communication network and collectively as a communication system. Using multiple types of network connections can allow a more cost-effective way to communicate information to the controller 120. For example, the complexity of the communication network used for each monitoring and control device in a particular control system configuration can be selected based upon the devices' particular communication requirements, thus minimizing expensive complex network connections when less expensive options are available.

[0027] The controller 120 controls and manages the utility tower 115 functionality to implement a programmed process for the bioreactors 105, 110. The controller 120 includes interface hardware and logic (e.g., hardware, software and/or firmware) for each type of network bus connection 135, 140, 145. The controller 120 also contains hardware and logic that receives information from the utility tower 115 and uses the information to monitor the bioreactors 105, 110 and control devices that affect the conditions in the bioreactors 105, 110 in accordance with instructions previously entered by a user, for example, in the form of a computer program, or commands that are entered interactively by the user. The controller 120 can also contain additional control and management functionality, for example, for logging a history of the process conditions, conducting trend analysis, running diagnostics, performing maintenance of the control system, documenting specified events, collecting audit trails on devices, requiring user authorization, and performing change management.

[0028] A user typically interacts with the controller 120 through a device connected to the utility tower 115, as described above. However, in another embodiment the

controller 120 can be connected to another device, for example, a stand-alone personal computer ("PC"), that allows the user to interact with the controller 120 by receiving information from the PC's display screen and inputting information through the PC's keyboard or mouse. To increase the reliability of the control system 100, the controller 120 typically includes one or more sets of redundant hardware components that operate with one component "active" and the other component in "standby." When the controller 120 includes redundant components, it can be configured so that if an active component fails, its corresponding standby component automatically becomes active and runs the functionality that was being run by the failed component. One example of a suitable controller 120 is the DeltaV™ MD Controller from Emerson Process Management.

[0029] Exemplary ways of using and constructing embodiments of the control system 100 are described in detail below with reference to Figures 2-7, which depict specific embodiments of the control system. Of course, because there are multiple ways to implement the control system, the following description should not be taken to limit the full scope of the invention.

Illustrative Embodiment

[0030] Figure 2 is a more detailed block diagram of an example of the control system of Figure 1. The control system is configured to control two bioreactors, in this example. The control system shown in Figure 2 controls the processes occurring in two bioreactors 220, 220' that are used for cell cultures. The bioreactors 220, 220' are sometimes referred to herein as benchtop bioreactors as they are generally sized to fit on a bench or laboratory table. Of course, the bioreactors 220, 220' can be placed in any convenient location, e.g., the floor, and be sized according to the process requirements. While this illustrative embodiment relates to a control system that runs, monitors, and controls a cell culture process, the control system can also be used for a variety of other processes that require monitoring process conditions and providing gasses, fluids, solids, and agitation as required.

[0031] The bioreactors 220, 220' can be glass or steel vessels and can be of various sizes to contain, for example, a fraction of a liter of solution or twenty liters or more

of solution. The top or headplates and the various orifices and fittings of the bioreactors 220, 220' are typically metal and can be manufactured from 316L stainless steel. The bioreactors 220, 220' are configurable in a variety of ways depending on the requirements of the application. For example, for growing cell cultures and microbial fermentation, the bioreactors 220, 220' can be configured with sensors for measuring conditions of the contained solutions, an agitation device, and orifices or fittings connected to lines for adding fluids, for the intake and exhaustion of gases or for extracting samples. According to an embodiment for processing cell cultures, a bioreactor can include the following components: glass or steel vessel, headplate, motor coupler, marine impeller, pH housing, dissolved oxygen (DO) housing, thermowell, sparger pipe, air overlay pipe, triple port, septum holder, sample pipe, and a stand. According to an embodiment for microbial fermentation, the bioreactor can include the following components: glass or steel vessel, headplate, motor coupler, rushton impeller, pH housing, thermowell, heat exchanger, baffles, triple port, septum holder, sample pipe and a stand. In either aforementioned embodiment, the bioreactor can also include the following components: motor, level/foam sensor and cable, water jacketed vessel, pH electrode and cable, DO sensor and cable, temperature sensor and cable, heating blanket, and an air outlet condenser. Bioreactors and the components described herein are commercially available from Broadley-James of Irvine, California.

[0032] As shown in Figure 2, the control system includes a utility tower 115 and a controller 120 that manages (e.g., monitors, controls, and documents) conditions in two bioreactors 220, 220'. The controller 120 includes functionality that determines what control actions are required, e.g., what services the utility tower 115 should provide to the bioreactors 220, 220', described in more detail hereinbelow. The controller 120 can determine control signals corresponding to the control actions that control the utility tower 115 to provide, for example, a fluid, gas or agitation to the bioreactors 220, 220', based on a programmed bioreactor process and/or based on information the controller 120 receives from the utility tower 115. When a controller 120 manages more than one bioreactor, it can determine control actions and a corresponding set of control signals for each bioreactor it manages. Functionality limiting access to the control system to authorized persons and requiring

electronic signatures, for example, user names and passwords, for certain actions can also be included on the controller 120.

[0033] The utility tower 115 includes a bioreactor monitoring system that can monitor the bioreactors 220, 220' and send information related to the bioreactors 220, 220' to the controller 120. In this example, the monitoring system includes dissolved oxygen transmitters 205, 205', pH transmitters 210, 210', and temperature transmitters 215, 215' that monitor conditions in the two bioreactors 220, 220', respectively. The utility tower 115 also includes a substance supply system which can supply a gas, fluid or solid to the bioreactor. In this example, the utility tower 115 includes a gas control system 235 and a pump control system 240 which are configured with a separate set of equipment to support each bioreactor 220, 220', described further below. The utility tower 115 also includes an agitation system which can agitate the bioreactors. In addition to simply agitating the solution in the bioreactors 220, 220', the agitation system can change the partial pressure of the dissolved oxygen in the media by the level of agitation applied. For example, increasing the level of agitation breaks the larger bubbles of air or oxygen enriched air, that is being provided to the bottom of the bioreactor, into smaller bubbles. It follows that this increases the total surface area of the oxygen bubbles and allows more oxygen into the media. In this example, the agitation system includes attached agitation units 260, 260'. Typically, the configuration of the monitoring system, the substance supply system, and the agitation system are similar for each bioreactor, however, they can be configured so each bioreactor 220, 220' is supported with different transmitters, different agitation units and different configurations for systems supplying gas, fluid, or solids in order to support two different applications. In other embodiments, a utility tower can be configured to support more than two bioreactors. Although sometimes referred to herein in the singular for ease of reference, the devices, systems, and modules described herein are applicable for monitoring and controlling both bioreactors 220, 220'.

[0034] As illustrated in the embodiment shown in Figure 2, the utility tower 115 and the controller 120 communicate using multiple busses 135, 140, 145. Although shown as wired busses in Figure 2, one or more of the busses 135, 140, 145 can be implemented using wireless links. In this embodiment, the utility tower 115 communicates information

from the DO transmitters 205, 205', the pH transmitters 210, 210', and the temperature transmitters 215, 215' to the controller 120 through a H1 FOUNDATION™ fieldbus 135. FOUNDATION™ fieldbus is an all-digital, serial, two-way communication network that can communicate multiple variables from one field device over the same pair of wires. The H1 implementation of FOUNDATION™ fieldbus works at 31.25 Kbit/sec and can connect to multiple field devices providing communication and power over standard twisted pair wiring. FOUNDATION™ fieldbus technology is known in the art and commercially available from Emerson Process Management in Austin, Texas.

[0035] In this example, the computer 225 communicates with the controller 120 over an Ethernet bus 140, a well known and relatively inexpensive digital network. For example, Ethernet is used by the computer 225 to communicate commands and instructions received from an operator using a local input device 280, for example, a keyboard, a mouse, or a wireless computing device, to the controller 120. The controller 120 includes a Ethernet switch/hub 265 that allows the computers of multiple utility towers to be connected and controlled by a single controller 120.

[0036] The gas control system 235, the pump control system 240 and the agitation units 260, 260' communicate with the controller 120 through a DeviceNet Gateway 230 and a DeviceNet bus 145, according to this embodiment. DeviceNet is a low-cost communications link typically used for connecting industrial devices (such as limit switches, photoelectric sensors, valve manifolds, motor starters, process sensors, bar code readers, variable frequency drives, panel displays and operator interfaces) to a network to eliminate expensive hardwiring. The direct connectivity of the DeviceNet bus can provide improved communication between devices as well as important device-level diagnostics not easily accessible or available through hardwired I/O interfaces. DeviceNet gateways and networks are well known in the art and are available from Interlink BT in Pennsylvania. In another embodiment, the gas control system 235, the pump control system 240 and the agitation units 260, 260' communicate with the controller 120 using a Profibus DP Gateway and a Profibus bus instead of the DeviceNet Gateway 230 and DeviceNet bus 145. Profibus buses are known in the art and are available from Interlink BT in Pennsylvania.

[0037] The control system can include functionality for measuring the dissolved oxygen in each bioreactor 220, 220'. In this example, the utility tower 115 includes two dissolved oxygen ("DO") transmitters 205, 205' configured such that each DO transmitters 205, 205' receives information from a DO sensor in one of the bioreactors 220, 220'. Although either the percentage of dissolved oxygen or the partial pressure of dissolved oxygen can be calculated by the DO transmitters 205, 205', in this example the partial pressure of dissolved oxygen is calculated. During calibration of the DO sensor, the DO transmitter 205 calculates and saves dissolved oxygen span and slope measurements that set the offset of the sensor to zero and calculate the value for a 100% signal from the sensor. The DO sensor is configured to contact the solution in the bioreactor 220 and communicate analog signals to the DO transmitter 205 related to the dissolved oxygen in the solution and the temperature of the solution. The DO transmitter 205 converts the analog signals to digital signals and calculates the partial pressure of dissolved oxygen of the solution. The DO transmitter communicates a value related to the actual output signal of the DO sensor, temperature information, a value related to the partial pressure of oxygen, and the slope and span calibration values as multiple channel digital data to the controller 120 over the FOUNDATION™ fieldbus 135. A dissolved oxygen sensor and dissolved oxygen transmitter as described above are commercially available from Broadley-James of Irvine, California and Emerson Process Management of Irvine California, respectively.

[0038] The control system can also measure the temperature of the solution in each bioreactor 220, 220' and communicate temperature information to the controller 120. The utility tower 115 includes two temperature transmitters 215, 215', which receive information from remote temperature devices ("RTD") in the bioreactors 220, 220', respectively. The RTD includes a single temperature sensors that provide an analog signal to the temperature transmitter 215 indicating a temperature measurement of the solution in the bioreactor 220. In another embodiment, the RTD includes two temperature sensors and provides two temperature measurements. The temperature transmitter 215 converts the received analog signals to digital signals, and calculates the "drift" of the first temperature measurement using the second temperature measurement. The temperature transmitter 215 communicates temperature information, including the first and second temperature

measurements, the status of the RTD (i.e., whether it is in or out of range), and the calculated temperature "drift," to the controller 120 over the FOUNDATION™ fieldbus 135. A RTD as described herein is commercially available from Burns Engineering of Wisconsin. A temperature transmitter as described herein is available from Emerson Process Management of Minnesota.

[0039] The control system also includes functionality that measures the pH of the solution in each bioreactor 220, 220'. The pH transmitters 210, 210' communicate pH information from pH sensors located in the bioreactors 220, 220' to the controller 120. A pH sensor in each of the bioreactors 220, 220' sends an analog signal that is related to a pH measurement of 0-14 to its corresponding pH transmitter 210, 210'. The pH transmitter 210 can analyze the raw pH signal received from the pH sensor and other data, including values for span and offset obtained from calibration of the pH sensor, the reference impedance, and the glass impedance, to determine if they are within specified range. The pH transmitter 210 converts the analog signal from the pH sensor to a digital signal, and communicates values related to span, offset, the raw signal from the pH sensor, pH value, reference impedance, and glass impedance to the controller 120 through the FOUNDATION™ fieldbus 135. A pH sensor as described herein available from Broadley-James of Irvine, California. A pH transmitter 210 as described herein are commercially available from Emerson Process Management of Irvine, California respectively.

[0040] Agitation units 260, 260' are included in the control system and provide agitation to the solutions contained in the bioreactors 220, 220'. In this example, the agitation unit 260 includes an impeller that is immersed in the solution, a motor that drives the impeller and a digital motor controller. The agitation motor signal comes off the motor via a digital encoder and goes to the motor controller. The digital motor controller signal (e.g., RPMs of the motor) goes to the DeviceNet gateway 230 which then sends the data through the DeviceNet bus 145 to the controller 120. As such, the controller 120 is then able to control and adjust the agitation unit 260 based on the needs of the process or changes by the operator. The agitation units 260, 260' are available from Maxon Motors, Switzerland.

[0041] As shown in Figure 2, the control system includes an embedded personal computer ("PC") 225 in the utility tower 115. The computer 225 can be a uni-processor or

multi-processor machine, and include an addressable storage medium or computer accessible medium, for example, random access memory (RAM), and a hard disk and/or removable media, e.g., floppy disks, laser disk players, digital video devices, compact disks, or magnetic optical tapes. The computer 225 can execute an appropriate operating system such as Linux, Unix, any of the versions of Microsoft Windows, Apple MacOS, IBM OS/2 or any other operating system that can operate compatibly with the software running on the controller 120. The computer 225 includes logic that runs the HMI, displaying, for example, system information received from the controller 120 or information received from an input device. If the HMI is a touchscreen, the computer 225 includes logic which manages its input/output functionality. The computer 225 also includes logic which communicates an operator's commands received from an input device or a touchscreen to the controller 120 over the Ethernet bus 140. The computer 25 can also include, among other things, functionality for tracking and electronically logging historical system data, obviating the need for paper-based operator logs. Although the computer 225 is shown in this example to be contained in the utility tower 115, in other embodiments it could be located with the controller or as a separate unit in communication with the controller. The computer 225 is described further in connection with Figure 6.

[0042] A gas control system 235 contained in the utility tower 115 provides the bioreactors 220, 220' with gasses, for example, air, oxygen, nitrogen, and carbon dioxide, as required for a particular application. The gas control system 235 can provide a single gas or a mixture of two or more gasses. Sources for the gasses are connected to input fittings in the utility tower 115. Gas control instructions which are included in the process control program running on the controller 120 and/or instructions interactively entered by an operator, control the gas control system 235 to provide a desired type of gas in a measured quantity to the bioreactors 220, 220'. The gas control system 235 provides the desired gas to either the "head space" of the bioreactors 220, 220' or to "sparge," i.e., so gas entering the bioreactors 220, 220' flows into the solution contained therein. The controller 120 communicates with the gas control unit 235 through the DeviceNet bus 145 and the DeviceNet Gateway 230, described further hereinbelow.

[0043] A pump control system 240 contained in the utility tower 115 provides the bioreactors 220, 220' with various types of fluids. Pump control instructions, included in the process control program running on the controller 120 and/or instructions that are interactively entered by an operator, control the pump control system 240 to provide a desired type of fluid in a measured quantity to the bioreactors 220, 220'. The pump control system 240 can be connected to a media vessel provided by the operator and used to pump the provided media into a bioreactor 220. Alternatively, the pump control system 240 can used to remove solution or media from the bioreactor 220 for testing or processing. The controller 120 communicates with the pump control system 235 through the DeviceNet bus 145 and the DeviceNet Gateway 230, described further hereinbelow. The pump control system 240 described for this embodiment and shown in Figure 2 and Figure 4 includes two pump heads, two pump motors and two pulse amplification circuits for each bioreactor 220, 220'. In other embodiments, the pump control module 240 can include one pump or more than two pumps for each bioreactor 220, 220'.

[0044] The control system can be configured to support many different applications, for example, controlling a process in a chamber or another enclosed or controlled environment, and which may require the devices and systems described herein, and/or other suitable monitoring devices and systems which are controllable to affect the particular application. To support other applications, the utility tower 115 can be configured with suitable transmitters that allow other sensors and analyzers to be coupled to the utility tower 115, instead of, or in addition to, the above-described sensors, including, e.g., for carbon dioxide, pressure, or conductivity. The utility tower 115 receives signals from the other sensors and analyzers coupled to the utility tower 115 and sends information related to the signals to the controller 120 over the first communication network 135.

[0045] In another embodiment, the control system can survey, electronically record and display information from other devices. For example, the control system can receive data from and control one or more stand-alone devices 255, 255'. Examples of a stand-alone device 255 include a device for measuring glucose, carbon dioxide, cell count, and cell viability of the solution in the bioreactors 220, 220', banks of peristaltic pumps that are outside of the utility tower, or a weigh scale. A stand-alone device 255 may include a

connection 270 to the bioreactor 220 that allows the device to retrieve a sample, or a connection 270 to a sensor in the bioreactor 220. Alternatively, a stand-alone device 255 may require the sample to be placed in the device.

[0046] The manner of coupling a stand-alone device 255 to the control system depends on its particular configuration. The stand-alone device 255 can be coupled directly to the communication system for direct communication with the controller 120 if its output is compatible with, for example, FOUNDATION™ fieldbus 135. For example, a device 255 that monitors cell count and cell viability can provide data, for example, the number of cells per a designated quantity, cell size, percentage of cell viability, total number of cells, and an image of the cells in the sample, directly to the controller 120 via the Foundation™ fieldbus. Alternatively, the output of the stand-alone device 255 can be coupled to a suitable transmitter in the utility tower 115, and the utility tower 115 can be configured to send information relating to the data from the stand-alone device 255 to the controller 120 via the FOUNDATION™ fieldbus 135. When the output of the stand-alone device 255 is not directly compatible with a transmitter or the communication system of the control system, for example, the output signal from a glucose analyzer through a RS232 connection, a converter may first be required to change the output signal from the stand-alone device 225 to a compatible signal.

[0047] In another example embodiment, the utility tower 115 can also be configured with devices 250, 250' which can be, for example, temperature control systems. The devices 250, 250' are coupled to discrete I/O blocks in the utility tower 115, and the discrete I/O blocks are coupled to the DeviceNet Gateway 230. The utility controller 120 communicates information for controlling these devices 250, 250' with the utility tower 115 via the DeviceNet bus 145. For example, to control a temperature control system, the controller 120 can receive temperature information related to the media in a bioreactor 220 from the utility tower 115 via the FOUNDATION™ fieldbus 135, determine if the media temperature should be increased or decreased, generate the corresponding control signal to increase or decrease the temperature of the media, and communicate the control signal to the utility tower 115 via the DeviceNet bus 145. In response to the control signal the utility tower 115 receives from the controller 120, the utility tower 115 communicates a signal, via

the DeviceNet Gateway 230 and the discrete I/O block, to the temperature control system to increase or decrease the temperature of the media.

[0048] One example of a temperature control system is a "cold finger" which is generally used to remove heat from the media. In this example, the cold finger is connected to a water source and a water drain line, and it is placed into the bioreactor so that the cold finger contacts the media. A controllable valve (not shown), which is positioned between the water source and the cold finger and can be modulated to control the flow of water through the cold finger, can be connected to an discrete I/O block in the utility tower 115. The discrete I/O block is coupled to the DeviceNet Gateway 230. The controller 120 sends control signals to the controllable valve to open or shut the valve, thus increasing or decreasing the flow of water through the cold finger and correspondingly increasing or decreasing the amount of cooling provided by the cold finger.

[0049] Another example of a temperature control system is a double-walled vessel system where water is circulated between the walls to provide both heating and/or cooling of the media to maintain a desired temperature. The double-walled vessel system can be coupled to an appropriate controller, which is coupled to the DeviceNet Gateway 230, and the controller provides the double-walled vessel system with a variable signal (e.g., 0-5 volts) that controls the temperature of the of the double-walled vessel system. The controller 120 receives temperature information related to the media and sends temperature control signals to the utility tower 115, as described above, and the utility tower 115 provides the variable signal to the double-walled vessel system via the DeviceNet Gateway 230 and the controller coupled to the double-walled vessel system .

[0050] In another example of a temperature control system is a "heating blanket" which wraps around the bioreactor. In this example, the heating pad is coupled to the utility tower 115, which provides power to the heating blanket and controls the on/off state of the heating blanket. Typically, the heating blanket is coupled to a discrete I/O block which is coupled to the DeviceNet Gateway 230. The controller 120 receives temperature information related to the media and sends temperature control signals to the utility tower 115, as described above. In response to the control signals, the utility tower 115 controls the heat provided to the media from the heating blanket, via the DeviceNet Gateway 230 and the

discrete I/O block coupled to the heating blanket, by switching the heating blanket on and off.

[0051] In yet another example embodiment, a control system for high performance liquid chromatography ("HPLC") includes sensors coupled to corresponding transmitters in the utility tower 115 for monitoring pH, temperature, conductivity, and pressure of a HPLC separator (e.g., at its inlet and outlet). The utility tower 115 sends information related to these characteristics to the controller 120 via FOUNDATION™ fieldbus 135. It is contemplated that a HPLC control system can be configured to control, among other things, the pressure in a HPLC separator in various ways, including, for example, by regulating the pressure of fluid flowing into the separator, or through the use of a piston in the separating tube to force the fluid through the separating medium, or by moving a diaphragm in the separator tube to increase or decrease the pressure. To control the pressure in the separator, suitable control devices for controlling the fluid pressure, the piston, or the position of the diaphragm can be connected to the DeviceNet Gateway 230. The controller 120 can be configured to determine control signals to increase or decrease the pressure in accordance with a programmed process and/or monitored conditions of the separator (e.g., pressure) and send the control signals to the utility tower 115 via the DeviceNet bus 145. The HPLC control system can also include a fluid controller, functionally similar to the above-described gas MFC, to precisely regulate the amount of fluid flowing into the separator.

[0052] In another embodiment, a control system can be configured to support applications for the petroleum industry. For example, a control system can control a supply system, such as a peristaltic pump, to precisely administer additives for a petroleum product, such as the quantity of red dye added to gasoline, or other desired additives.

[0053] In the semi-conductor field, a control system can be configured to actively control gasses used for wafer production by monitoring the amount of gas in a process chamber with suitable sensors, and providing gasses to the process chamber based on the monitored gas levels and a defined process programmed into the control system. A control system supporting semiconductor fabrication can also include other specialized monitoring equipment, for example, temperature sensors that send temperature data of the chamber

and/or of the surface of the wafer to the utility tower 115, which passes information related to the temperature data to a controller 120 via the FOUNDATION™ fieldbus 135 as in input for the control process. A control system may also include heating and cooling devices (e.g., a quartz heater) that are coupled to the utility tower 115 via the DeviceNet Gateway 230, and controlled by signals sent from the controller 120 to the utility tower 115 via the DeviceNet bus 145 in accordance with the process steps and parameters programmed in the controller 120.

[0054] Additionally, the foregoing control system can be configured to help manage a supply and inventory process. In one example, the control system includes an input device, for example, a bar code scanner, coupled to the utility tower by a USB port at the interface connection 150 (Figure 1). Suitably coded consumables that are used in the process supported by the utility tower are identified by the bar code scanner, and the control system records and tracks which consumables have been used. In one example, the control system can send the information relating to the use of the consumable to another system, e.g., an inventory or supply system, via the Ethernet bus 140 or another suitable communication network, which can use the information to help manage the supply of consumables for the lab.

[0055] In another example configuration, the utility tower 115 can be coupled to a weigh scale 255, and the controller 120 is configured to use feedback from the weigh scale 255 to control the amount of fluid provided by the pump control system 240 or another substance delivery system. The weigh scale 255 can be positioned to weigh the bioreactor 220 or a substance, for example, a reagent, provided to the bioreactor 220. Alternatively, the weigh scale 255 can be configured to provide data via an output connection, for example, Profibus, that allows it to communicate directly with the controller 120 via a Profibus connection 135. In another example, the scale provides a stream of pulses where the rate of the pulses changes based on the weight measurement. In this latter example, the weigh scale is coupled and provides pulses to an I/O connection in the utility tower 115, which communicates the pulse information to the controller 120 via the DeviceNet bus 145. Based on the feedback from the weigh scale 255, the controller 120 can send a control signal to the

utility tower 115 to provide or remove a desired amount of fluid or media using the pump control system 240.

[0056] The control system can keep the solution in the bioreactor at a desired level that can be programmed into the controller 120 by using the pump control system 240. In one example configuration, the weigh scale 225 weighs the bioreactor 220, as described above, and the pump control system 240 receives control signals from the controller 120 to provide or remove fluid to maintain a desired level. In another example configuration, a level detector is coupled to a corresponding discrete I/O block in the utility tower 115 and provides information related to the level of the solution in the bioreactor 220. The utility tower 115 communicates solution level information to the controller 120 via the DeviceNet bus 145, and the controller 120 can send a control signal to the utility tower 115 to provide or remove a desired amount of fluid using the pump control system 240 to maintain the desired level. In another example configuration, the weigh scale 225 weighs the fluid removed from the bioreactor 220 and this information is communicated to the controller 120 by the utility tower 115 via the DeviceNet bus 145. The controller 120 can be programmed with the fluid's weight, determine the amount of fluid required to compensate for the fluid removed, and send a control signal to the utility tower 115 to provide the proper amount of fluid using the pump control system 240.

[0057] In another embodiment, the control system can use a gravity flow system to feed substances, including fluids, to the bioreactors. A second tower (not shown), referred to herein as an accessory tower, can be included in the control system and configured to include a coriolis meter (not shown) which provides precise metering for a gravity fluid flow. The accessory tower can be coupled to the utility tower 115 via the DeviceNet Gateway 230. Alternatively, the accessory tower can be connected to the controller 120 over a DeviceNet bus 145. In either configuration, the controller 120 receives fluid flow information from the accessory tower and sends signals to the accessory tower that control the flow of the fluid via the DeviceNet bus 145. The accessory tower, when suitably positioned relative to the bioreactor, thus provides a controlled fluid flow to the bioreactor with out the use of a pump. In another embodiment, the control system can include a pump control system 240

configured to provide a fluid to a bioreactor 220 using compressed air to facilitate the flow of the substance to the bioreactor 220.

[0058] Turning now to Figure 3, the gas control system 235 is shown in further detail, according to one embodiment. The gas control system 235 contains two sets of gas control devices, each set supporting one of the bioreactors 220, 220'. For example, one bioreactor 220 is supported by a first set of thermal mass flow controllers 304, 306, 308, 310, 312, valves, for example, solenoid check valves 324, 326, 328, 330, 332, and directional three-way valves, such as three-way solenoid valves 344, 346, 348. Similarly, a second bioreactor 220' is supported by a second set of mass flow controllers 314, 316, 318, 320, 322, solenoid check valves 334, 336, 338, 340, 342, and directional three-way solenoid valves 350, 352, 354.

[0059] Supply lines for oxygen, nitrogen, carbon dioxide and air are connected to input fittings (not shown) on the utility tower 115. As shown in Figure 3, oxygen, nitrogen and carbon dioxide can have a similar gas flow path through the gas control system 235. For example, oxygen flows through the solenoid check valve 326, through the thermal mass flow controller ("MFC") 306, and then through the directional three-way solenoid valve 344 which directs the oxygen to a connection with the head space h or sparge s of the bioreactor 220. The solenoid check valves 324, 326, 328, 330, 332, 334, 336, 338, 340, 342 receive open and close control signals from the controller 120 via from a relay discrete I/O (not shown), which is connected to the DeviceNet Gateway 230 (Figure 2).

[0060] According to one embodiment, the gas control system 235 includes five MFC's, one MFC each for oxygen 306, nitrogen 308, carbon dioxide 310, and two MFC's for air 304, 312. In other embodiments, the gas control system 235 can be configured to have fewer or more MFC's, and different gases may be desired and appropriately used instead of the aforementioned gases. Each MFC includes a measuring element that measures the amount of gas passing through the MFC and an electrically actuated solenoid valve that modulates to let the gas flow through the MFC based on a control signal the MFC receives from the controller 120 via the DeviceNet Gateway 230. The MFC also includes a transmitter that sends the position of the solenoid valve, the gas flow rate measurement, and the temperature of the gas to the controller 120 via the DeviceNet Gateway 230. Typically,

closing the solenoid valve in the MFC effectively shuts off 99.7% of the gas flow through the MFC. Using a separate solenoid check valve, such as solenoid check valve 326, ensures the gas flow is completely stopped and accordingly permits more accurate process control.

[0061] As illustrated in Figure 3, the three-way solenoid valves 344, 346, 348 direct the flow of oxygen, nitrogen, and carbon dioxide, respectively, to either the head space (indicated by "h") or sparge (indicated by "s") of a connected bioreactor 220. The gas control system 235 includes two MFC's 305, 312 for air. Air flowing through one MFC 304 flows to the head space of a bioreactor, while air flowing through the other MFC 312 provides air to sparge the bioreactor. The three-way solenoid valves 344, 346, 348, 350, 352, 354 receive signals to align the three way valve to either sparge or head space, or to close the valve from the controller 120 via a relay discrete I/O (not shown) which is connected to the DeviceNet Gateway 230. In one example, the gas control system 235 can provide two or more gasses to the bioreactor 220 by mixing the gasses in a common delivery tubing or manifold (not shown) before the gasses enter the bioreactor 220.

[0062] Figure 4 illustrates the pump control system 240 configured to control two pumps for each of the bioreactors 220, 220' (Figure 2), according to one embodiment. The pump control system 240 includes pump modules 405, 425, 430, 435, with pump module 405 shown expanded to provide more detail. The description hereinbelow is for pump module 405 but it also applies to the other pump modules 425, 430, 435 as they are typically configured. Pump module 405 includes a peristaltic pump 415 that is driven by a brushless motor 410. The peristaltic pump 415 moves fluid through a length of flexible tubing to a bioreactor by using rotors outside the tubing to push the fluid through the tube. The motor 410 and, correspondingly, the peristaltic pump 415, is controlled by varying the voltage applied to the motor 410, for example, between zero and four volts. In accordance to the process programmed into the controller 120, or in response to interactively entered pump control commands, the controller 120 causes the peristaltic pump 415 to provide fluid to the bioreactor by communicating a control signal to the DeviceNet Gateway 230, which controls the amount of voltage applied to the motor 410. The pump control system 240 can be used to provide fluid to or remove fluid (e.g., for harvesting, transferring, or sampling) from the bioreactor 220.

[0063] The pump module 405 includes a pulse amplification circuit 420 with connections 421, 422 to the wires supplying power to the motor 410. The pulse amplification circuit 420 detects and amplifies high frequency "pulses" that are generated by the motor 410 and provides the pulses as feedback to the controller 120. The number of pulses the motor generates is directly related to the movement of the motor, and, accordingly, the rotation of the pump. The controller 120 includes functionality that determines the number of pump revolutions per minute ("RPM") by counting the number of pulses it receives from the pulse amplification circuit 420. In this embodiment, for example, 32,000 pulses are equivalent to one revolution of the pump rotors. As the peristaltic pump 415 is calibrated to provide a known amount of fluid per revolution, the controller 120 can use the pulses as a feedback mechanism and thus more accurately control the amount fluid provided by the pump 415. For example, the typical accuracy of a peristaltic pump is within about 4-5% of the desired amount. By controlling the pump using the pulse amplification circuit 420, the accuracy of the peristaltic pump dramatically increases so that the provided amount of fluid is within about .5% of the desired amount. The calculated pump RPM can also be sent from the controller 120 to the embedded PC which displays the RPM on the HMI. A peristaltic pump as described hereinabove is available from Watson Marlow of Bredel, England.

[0064] Figure 5 illustrates a block diagram of the controller 120. One example of a suitable controller 120 is the DeltaV™ MD Controller from Emerson Process Management. According to one embodiment, the controller 120 includes DeltaV™ control system software 555 ("DeltaV") from Emerson Process Management. Alternatively, other suitable control system software incorporating the functionality described herein can also be used. The control system software 555 can include one or more subsystems or modules. As can be appreciated by a skilled technologist, each of the modules can be implemented in hardware or software, and comprise various subroutines, procedures, definitional statements, and macros that perform certain tasks. Therefore, the following description of each of the modules is used for convenience to describe the functionality of the control system. In a software implementation, all the modules are typically separately compiled and linked into a single executable program. The functionality described herein for each of the modules may be

arbitrarily redistributed to one of the other modules, combined together in a single module, or made available in, for example, a shareable dynamic link library. These modules may be configured to reside on addressable storage medium and configured to execute on one or more processors. Thus, a module may include, by way of example, other subsystems, components, such as software components, object-oriented software components, class components and task components, processes, functions, attributes, procedures, subroutines, segments of program code, drivers, firmware, microcode, circuitry, data, databases, data structures, tables, arrays, and variables.

[0065] To implement a particular bioreactor cell growth process, the control system software 555 is configured with the characteristics of the hardware and software for the desired control system. During configuration, a graphical representation of the control system is defined. The control system software includes images of equipment, e.g., check valves, three-way valves, pumps, tubing, vessels, etc., that are used to build a displayable representation of the desired control system. Characteristics of the control system equipment system that are required for control and communication are programmed into the control system software 555 and associated with the appropriate image. Once configured, the control system software 555 can display the representation of the control system or portions thereof, and information that relates to the control system, on the HMI or another suitable display device, while the control system is running the cell culture growth process. The information displayed can include, for example, temperature, pH, DO, agitation speed, valve alignment, headspace gas data, sparge gas data, pump data including revolutions and quantity, gas flow data.

[0066] The steps, parameters and conditions of the desired cell culture process are entered into the control system software 555. The steps, parameters and conditions can include, for example, defining when, in relation to time or to a monitored condition, and in what amount, gas, fluid, and/or agitation is provided to a bioreactor. Once a cell culture process is properly entered, the control system software can run the process in accordance with the predefined steps and conditions, consistently reproducing the process and electronically logging events and conditions occurring during the process.

[0067] The controller 120 includes a FOUNDATION™ fieldbus interface 505 connected to the FOUNDATION™ fieldbus 135, a DeviceNet interface 510 connected to the DeviceNet bus 140, and a Ethernet interface 515 connected to the Ethernet bus 145. The control system software 555 uses the interfaces 505, 510, 515 to communicate with the utility tower 115, the devices contained therein and attached thereto. In this embodiment, the control system software 555 receives information from the pH transmitters 210, 210' the temperature transmitters 215, 215', and the DO transmitters 205, 205' using the FOUNDATION™ fieldbus interface 505. The control system software 555 communicates with the DeviceNet Gateway 230 via the DeviceNet Interface 510, and communicates with the computer 225 via the Ethernet bus 140.

[0068] The control system software 555 can include a diagnostic and maintenance module 560 that runs diagnostic checks on the control system and alert the operator to maintenance actions that are required, including predictive maintenance actions. The control system software 555 can send the diagnostic and maintenance data to the computer 225, via the Ethernet bus 140, where the data can be stored in memory.

[0069] The control system software 555 can also include a module 550 that electronically logs events occurring in the control system, thereby eliminating the need to keep paper-based operator logs. For example, information that the control system software 555 receives from the utility tower 115 relating to the temperature, pH or the partial pressure of dissolved oxygen of the solution in the bioreactors can be electronically logged and date/time stamped. Events or control actions started or stopped by the control system software 555 can also be electronically logged and date/time stamped. For example, when the control system software 555 sends a signal to the utility tower 115 to provide gas, fluid or agitation to the bioreactors, the start and stop times for that events can be recorded by the event logging module 550. Information sent from the utility tower 115 to the control system software 555, relating to the amount of gas or fluid provided to the bioreactor, or the RPM's of an agitation unit, can also be electronically logged by the control system software 555 to maintain an electronic history of the process. The control system software 555 can send the electronic logs, via the Ethernet interface 515, to the computer 225 which stores them in memory, for example, on its hard disk. In other embodiments, the electronic logs may be

stored in other suitable locations, e.g., on a PC or a dedicated storage medium in communication with the controller 120.

[0070] In this illustrative embodiment, the controller 120 is configured with DeltaV control system software 555 which manages the cell culture process by monitoring and controlling the conditions in the bioreactor. To monitor the process, DeltaV 555 receives information relating to the conditions of the solution in the bioreactors. In this example, during the cell culture growth process DeltaV 555 receives temperature, pH, and dissolved oxygen information from the temperature transmitters 215, 215', pH transmitters 210, 210' and the DO transmitters 205, 205' via the FOUNDATION fieldbus interface 505. DeltaV 555 includes a temperature module 520, a pH module 525 and a dissolved oxygen module 530 which can process the information from the transmitters to determine if the temperature, pH and the DO of the solution are within parameters that were programmed while configuring DeltaV for the particular cell culture process. The temperature module 520, a pH module 525 and a dissolved oxygen module 530 can also provide the current temperature, pH, and DO for display on the HMI. If the temperature, pH or DO of the solution falls outside of its parameters, DeltaV 555 can determine whether to execute a control action, for example, providing gas, fluid or agitation to the solution, to bring the condition back within its parameters.

[0071] DeltaV 555 can include an agitation control module 535 that can send a control signal via the DeviceNet interface 510 to cause an agitation unit to agitate the media in the bioreactor 220. In many cell culture and microbial fermentation processes, agitation is provided continuously or nearly continuously. The agitation control module 535 can also send the agitation control signal as part of the normal programmed cell culture process, i.e., if agitation is required at a specified time in the process. Or, the agitation control module 535 can send an agitation control signal based on a monitored condition relative to a specified set-point that is programmed into DeltaV, e.g., the level agitation can be increased or decreased as the monitored condition becomes closer to or further from the specified set-point. Alternatively, the agitation control module 535 can control an agitation unit to provide agitation to the solution based on commands that are interactively entered by an operator on the HMI or by another input device.

[0072] In this example, DeltaV 555 also contains a gas control module 545 that sends control signals via the DeviceNet interface 510 to cause the gas control system 235 (Figure 3) to provide gas to the bioreactor to, for example, change a chemical characteristic of the solution in the bioreactor e.g., pH. In this embodiment, the gas control module 545 can provide air, oxygen, nitrogen, carbon dioxide or a mixture of any of the gasses to the head space or sparge of the bioreactor. For example, to provide oxygen to a bioreactor, the gas control module 545 can send control signals to the gas control system 235 (Figure 3) that open the oxygen check valve 326, open the valve in the oxygen MFC 306, and open the oxygen directional three-way solenoid valve 344, allowing gas to flow to either head space or sparge. The gas control module 545 can determine the amount of oxygen being provided to the bioreactor by processing gas flow information it receives from the MFC via the DeviceNet Gateway 230. When the desired amount of oxygen has been provided, the gas control module 545 sends control signals via the DeviceNet Gateway 230 to close the oxygen solenoid check valve 326, the valve in the oxygen MFC 306 and oxygen directional three-way valve 344. The gas control module 545 can also change the gas flow rate as a result of information that the controller 120 receives, e.g., information related to the partial pressure of oxygen or pH of the media. For example, to control the partial pressure of oxygen, the gas control module 545 can increase the rate that the gas control system 235 provides oxygen to the bioreactor 220 as the difference between the monitored partial pressure and the desired partial pressure increases, and correspondingly decrease the rate that the gas control system 235 provides oxygen to the bioreactor 220 as the difference between the monitored partial pressure and the desired partial pressure decreases.

[0073] The control system software 555 contains a pump control module 540 that can send a control signal via the DeviceNet interface 510 to cause the pump control system 240 (Figure 2) to provide a fluid to the bioreactor to, for example, change a chemical characteristic of the solution in the bioreactor, or change the temperature of the solution by providing fluid to circulate in a water-jacketed bioreactor vessel or by directly introducing a fluid into the solution. The pump control module 540 can increase or decrease the rate at which a fluid is provided to a bioreactor 220 in response to a measured condition, e.g., pH, in the bioreactor 220. Each revolution of the rotors of the peristaltic pump in the control system

causes a known and consistent amount of fluid to flow through the tube connected to the pump. The characteristics of a peristaltic pump, including its fluid flow per rotor revolution and the number of high frequency pulses associated with each rotor revolution, can be programmed into DeltaV 555 during the control system configuration. When the peristaltic pump is activated, the pump control module 545 receives, via the DeviceNet Gateway 230, high frequency pulses from the pulse amplification circuit 420 (Figure 4), described hereinabove. The pump control module 545 uses the number of pulses to determine the number of revolutions the pump has made, and accordingly, to determine the precise amount of fluid the pump has provided to the bioreactor.

[0074] Figure 6 further illustrates the computer 225 that can be included in a utility tower 115 (Figure 2). In this embodiment, the computer 225 includes volatile memory 605, e.g., random access memory, and non-volatile memory 625, e.g., a hard disk. The computer includes a network interface 615, e.g., an Ethernet interface, to communicate with the controller 120. The computer 225 can run a Windows type-operating system, another operating system that is operationally compatible with the operating system run on the controller 120 and the control system software. The computer can also includes a user interface module 630 which manages the data input to the control system from, for example, a touchscreen HMI, a wireless device, a keyboard, or a mouse. The user interface module 630 provides the data as necessary to the controller 120 via the network interface 615.

[0075] The computer 225 can include a Data History and Trending module 620 which can store an electronic history of a process in the memory of the computer or use the electronically logged data to show trend information. Typically, the computer 225 interacts with the controller 120 to electronically record the history of the processes of the one or two bioreactors 220, 220' attached to the utility tower 115 containing the computer 225. The electronic history can include the temperature, pH, and dissolved oxygen information transmitted from the utility tower 115 to the controller 120 during the cell culture process. The history can also include a detailed log of the events that occurred during a process, for example, the amount and type of fluid or gas provided to a bioreactor and when it was provided, or the duration of agitation provided to a bioreactor, the speed of the impeller, and the time the agitation was provided. The data history and trending module 620 further allows

analysis of the logged history to develop historical trending which can be used for planning subsequent processes.

[0076] The computer 225 can also include a batch module 625 that interacts with the controller 120 via the network interface 615 to allow a sequence of steps to be run as without requiring an operator's input at every step or without reprogramming the control system software. For example, the sequence can include steps to fill a vessel with a specified amount of fluid, activating a pump to fill the vessel and turning the pump off when the vessel is complete. The batch module 625 allows the operator to employ the control mechanisms incorporated in the utility tower 115 and the controller 120 for tasks typically accomplished imprecisely by an operator. When the batch module 625 is running, the steps executed by the batch module 625 take priority over preprogrammed steps in the control system software.

[0077] The computer 225 can include one or more optional modules (not shown), depending on the desired system configuration. For example, an optional module can include neural network functionality that can model the behavior of a bioreactor process to help forecast the values of certain process measurements and facilitate predictive process control. The computer 225 can also include a module that allows increased functionality of the user interface, for example, allowing the use of a virtual keyboard from a touchscreen HMI.

[0078] Figure 7 illustrates a example configuration for networking multiple utility towers and controllers. In this example, Segment 1 includes ten utility towers 115a-j, each supporting two bioreactors 220, 220'. Ten utility towers 115a-j connect to controller 120 by three busses 720, which are, in this example, FOUNDATION™ fieldbus, DeviceNet, and Ethernet. Segment 2 includes a similar configuration of utility towers 115k-t that each support two bioreactors 220, 220', and connect to controller 120' busses 720', which are also, in this example, FOUNDATION™ fieldbus, DeviceNet, and Ethernet. The controllers 120, 120' are connected by cables 715 which are, for example, FOUNDATION™ fieldbus, DeviceNet, and Ethernet. In this way, two controllers 120, 120' can network up to 40 bioreactors. Additional segments containing a controller, utility towers, and bioreactors can be added to the network connections 720 to create an even larger application suite of networked benchtop bioreactors. In different embodiments, other types of network busses may be used. For example, Profibus can be used instead of DeviceNet. Additionally,

although the network in Figure 7 is illustrated with wired connections between the controllers, utility towers and the bioreactors, a suitable wireless technology can also be effectively used for any of these connections.

[0079] The foregoing description details certain embodiments of the invention. It will be appreciated, however, that no matter how detailed the foregoing appears in text, the invention can be practiced in many ways. As is also stated above, it should be noted that the use of particular terminology when describing certain features or aspects of the invention should not be taken to imply that the terminology is being re-defined herein to be restricted to including any specific characteristics of the features or aspects of the invention with which that terminology is associated. The scope of the invention should therefore be construed in accordance with the appended claims and any equivalents thereof.